

A2
cont

(iii) a syndecan-4 cytoplasmic portion present within the cytoplasm of a transfected vascular endothelial cell which is joined to said transmembrane portion and said extracellular N-terminal portion of said expressed proteoglycan entity, said syndecan-4 cytoplasmic portion being the expressed product of at least one third DNA sequence in the constructed expression vector coding for the cytoplasmic domain of the syndecan-4 molecule of said proteoglycan entity expressed by a transfected vascular endothelial cell in-situ after being transfected with said third DNA sequence; and

allowing said transfected vascular endothelial cells bearing said overexpressed extracellular matrix proteoglycan entities to stimulate angiogenesis in-situ.

REMARKS

The substance of the non-final Official Action mailed January 24, 2000 may be summarized as follows: The Examiners have stated that applicants' election with traverse on the grounds that claims 1-19 represent a single inventive entity was not found persuasive and the Examiners have made final the restriction of original claim 18 as a different invention. In addition, the Examiners have found that the pending application presently fails to satisfy the requirements regarding nucleotide sequence and/or amino acid sequence disclosures and that applicants must now comply with the proper sequence rules as set forth in 37 C.F.R. 1.821-1.825 respectively. Finally, the Examiners have rejected original claims 1-17 and 19 under 35 U.S.C. 112, second paragraph as being indefinite in language for specifically stated reasons. In response, applicants have canceled original claim 18, without prejudice; amended original claims 1-3 and 12-14 respectively; have presented documentation for and disclosures of the relevant nucleotide sequences and/or

amino acid sequences in conformity with 37 C.F.R. 1.821-1.825 respectively; and, in fulfillment of applicants' duties, enclose herewith photocopies of the International Search Report as prepared by the International Searching Authority of the PCT. By these cancellations, amendments, and enclosures, applicants believe they have overcome and obviated each basis for objection and rejection stated by the Examiners in the present non-final Official Action.

In view of the Examiners' stated views and positions in this non-final Official Action, applicants will provide the sum and substance of the various issues in controversy and the manner in which each has been resolved individually.

1. Initially, regarding the Examiners' final restriction of original claim 18 as defining a different invention, applicants reluctantly acknowledge the Examiners' decision and have canceled original claim 18, without prejudice, from the present application. Accordingly, original claim 18 stands withdrawn from further consideration as a non-elected invention.

2. As regards the non-compliance with the rules of proper disclosure for nucleotide sequences and/or amino acid sequences presented within the Specification of the present application, applicants have enclosed the following: a paper form copy of the "Sequence Listing" to be formally entered into the original Specification; an Amendment of Specification and Request for Entry of a paper form copy of the sequence listing; a computer readable form copy of the "Sequence Listing"; and a Statement and Verification of Substantive Identity between the computer readable form copy and the paper form copy of the "Sequence Listing". The submission of this diskette and documents in this manner

completely satisfies and complies with the requisite rules, 37 C.F.R. 1.821-1.825 in their entirety. Applicants have also returned a copy of the Notice To Comply as part of these enclosures. Accordingly, applicants believe they have complied with all requisite requirements for patent applications containing nucleotide sequences and/or amino acid sequences; and properly amended the present Specification in the appropriate manner to indicate such compliance.

3. As regards the rejection of original claims 1-17 and 19 under 35 U.S.C. 112, second paragraph, applicants have noted and acquiesced to the Examiners' stated position and view that original claims 1-2 and 12-14 are deficient in language for the reasons stated by the Examiners. Accordingly, each of independent claims 1-2 and 12-14 have been amended to explicitly recite that the transfected endothelial cells are those cells transfected with the recited DNA segments. Such indefiniteness as may have existed previously has therefore been removed; and these independent claims now define the present invention accurately and precisely in definite terms.

Also, as regards the vagueness of language in original claim 3, applicants have deleted the word "on" which is erroneous and believed to have been a typographical error in the original text. Such other amendments as are now made within the language of claim 3 merely correct the existing language to conform precisely and consistently in wording throughout the entirety of the claim itself.

As regards original claim 9 [and its counterpart, original claim 10], applicants respectfully submit that the Examiners are in error. Attention is directed to the antecedent claim reference of original claim 9, independent claim 3. It will be noted and appreciated

that the wording of independent claim 3 recites and refers to an "in-situ transfected endothelial cell... ."; and that the entirety of claim 3 defines the transfected endothelial cell as always being "in-situ" as such. By definition, the term "in-situ" designates an entity in the natural or original position; and accordingly "in-situ" includes transfected endothelial cells which are found in-vivo [the natural life setting]], or ex-vivo [removed from the natural life setting] or in-vitro [in a artificially created viable setting]. It is within this definitional context that original dependent claims 9 and 10 have been presented. Thus, as stated by original dependent claim 9, the in-situ transfected endothelial cell exists under in-vivo conditions; alternatively, dependent claim 10 defines the in-situ transfected endothelial cell in an in-vitro condition.

The Examiners' stated view and position is thus erroneous in its entirety because the language of original claim 3 does not place the cell in any context exclusively as being "in-vivo", or "ex-vivo", or "in-vitro". The Examiners have apparently misread the explicit language of original claim 3 in this regard; and have misconstrued the precise meaning of the term "in-situ" too narrowly and erroneously by insisting on an "in-vivo" context. The Examiners' mistake is quite understandable, but is completely inaccurate and without any factual basis whatsoever.

Finally, the Examiners have stated that applicants have misspelled "heparin" as "heparan" throughout the claims and requested correction of this error. With all respect due to the Examiners, applicants respectfully submit that it is the Examiners who are in error. There is no misspelling error as such. To demonstrate the propriety of applicants' point and position, applicants have enclosed a copy of pages 710-711 from Saunders Dictionary & Encyclopedia; and direct the Examiners' attention to the information at page

710, right-hand column, last full paragraph which defines and describes the term "heparan" and distinguishes it from the term "heparin", which is different chemically, structurally, and compositionally as stated at page 711, left-hand column, first full paragraph. Applicants respectfully submit that the correct entity and chemical composition described in this application is solely and exclusively "heparan" and not "heparin". Accordingly, applicants submit there is no error and thus no correction of any words within the Specification or claims is necessary or required.

4. One additional matter requires attention. Applicants and their undersigned attorney have noted the absence in this non-final Official Action of any prior art references, publication citations, or even the form giving notice of specifically cited references. Accordingly, in keeping with and satisfying applicants' duty of candor and full disclosure, applicants have enclosed a photocopy of the International Search Report prepared by the International Searching Authority of the Patent Cooperation Treaty; and provide copies of each of the publications identified within that International Search Report. Applicants however, strongly disagree with the view that these cited documents are relevant; and believe that the individual publications listed within this International Search Report have little or no relevance or bearing on the present invention as defined by the claims now pending. Nevertheless, in keeping with their legal duty, applicants submit this document and copies of the referenced publications to the Examiners for their inspection and review.

Overall therefore, applicants respectfully submit that each basis of objection or rejection stated by the Examiners has been addressed and rectified by applicants as part of this Response. In particular, claim 18 directed to a non-elected invention has been

withdrawn; applicants have complied with the requisite rules, 37 C.F.R. 1.821-1.825; and each of claims 1-17 and 19 have been amended or shown to be both definite and precise in language which distinctly recites what the subject matter of the present invention is. For all these reasons, applicants respectfully submit that independent claims 1-3, and 12-14 as presently amended are therefore allowable.

In addition, claims 4-11 and claims 15-17 and 19 each depend from an independent claim and merely provide particular limitations and preferred embodiments to the unique and non-obvious invention defined therein. Since independent claims 1-3 and 12-14 are believed to be in condition for allowance and claims 4-11, 15-17, and 19 respectively depend therefrom, all of these claims are believed to be allowable.

In view of the above discussion and summary review, applicants believe that this case is now in condition for allowance and reconsideration is respectfully requested. The Examiners are invited to call applicants' undersigned attorney should they feel that such a telephone call would further the prosecution of the present application.

Respectfully submitted,
MICHAEL SIMONS
RUDIGER VOLK
ARIE HOROWITZ

By:



David Prashker
Registration No. 29,693
Attorney for Applicants
P.O. Box 5387
Magnolia, Massachusetts 01930
Tel.: (978) 525-3794